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EXAMINER	
MORRIS, PATRICIA L	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,788	DRYSDALE ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *14,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13 and 15-18 are under consideration in this application.

Claims 14, 19 and 20 are held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b).

Election/Restrictions

Applicant's election without traverse of Group I, example 14 and the method of treating cancer in the reply filed on November 4, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

This application has been examined to the extent readable on the elected compound wherein Ar^1 represents aryl and Q, R_2 –R4, R^A-R^C represent nonheterocyclic groups as set forth in claim 1, exclusively. Claim 12 has been examined to the extent readable on the treatment of cancer.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Abbas et al. (Journal of Chemical Research. Synopses, 4. 124-125 2001)) and Dyachenko et al. I (Chemistry of Heterocyclic Compounds, 34 (2), 1998, 188-194), II (Russian Journal of Organic Chemistry, 33(7), 1997, 1014-1017).

Abbas et al. specifically recites the instant compound wherein Ar^1 is 4-hydoxy phenyl, R_3 is NH_2 and R_4 is carboxamide. Note compound 18b in Scheme two therein.

Dyachenko et al. I disclose the instant compound wherein Ar^1 is 4-butoxyphenyl, R_3 is NH_2 and R_4 is $-CONR^B(Alk_n)R^A$ wherein R^B hydrogen, n is 0 and R^A is phenyl. Note compound XIIIa on page 189 therein.

Dyachenko et al. teach the claimed compound wherein Ar^1 is 4-bromophenyl, R_3 is NH_2 and R_4 is carboxamide. Note compound IXb in scheme 1 on page 1015 therein.

Hence, the instant compounds are deemed to be anticipated therefrom.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Abbas et al. and Dyachenko et al. I, II.

As discussed supra, Abbas et al. and Dyachenko et al. I, II teach specific compounds that are disclosed herein.

Also, the prior art compounds differ from the compound claimed herein as a halogen analog, a positional isomer and alkyl homolog of the claimed compounds. For example, the claimed compounds wherein Ar^1 is phenyl substituted by chloro, fluoro or iodo would be a halogen or positional isomer of compound IXb of Dyachenko et al. II. The replacement of hydrogen by methyl of compound XIIIa of Dyachenko et al. is an optional obvious variation. The claimed compound wherein Ar^1 is 3-hydroxyphenyl would be a positional isomer of the compound of Abbas et al. One having ordinary skill in the art would have been motivated by the disclosure of the prior art compounds to arrive at other compounds within the claimed genus The motivation to make these compounds is their close structural similarities to the disclosed compound. While homology is considered to be present even if true "homology" is not present, such does not defeat the prima facie case of obviousness raised by the art. Attention, in this regard is directed to In re Druey et al., 50 CCPA 1538, 319 F.2d 237, 138 USPQ 39, wherein Judge Worley, delivering the Court's opinion, stated:

> "We need not decide here whether the compounds in question are properly labeled homologues. It appears to us from the authorities cited by the solicitor and appellants that the term homologue is used by chemists at times in a broad sense, and at other times in a narrow or strict sense. The name used to designate the relationship between the related compound is not necessarily controlling; it is the closeness of that relationship which is indicative of the obviousness or unobviousness of the new compound." 50 CCPA 1541.

Also, as the Court stated in In re Payne et al., 606 F.2d 302, 203 USPQ 245 at 255 (CCPA 1979):

> "the name used to designate the relationship between related compounds is not necessarily controlling; it is the closeness of that relationship which is indicative of the obviousness or unobviousness of the new compound."

In addition, any question of why would one conceive and use the similar compounds (i.e. "motivation") is answered by the Court in In re Gyurik et al., 596 F.2d 1012, 201 USPQ 552 at 557.

> "In obviousness rejections based in close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the prima facie case of obviousness, rises from the expectation that compounds similar in structure will have similar properties."

Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is a lack of description as to how the solvates and hydrates are produced and what solvates and hydrates are produced in the specification. Vippagunata et al. (Advanced Drug Delivery Reviews 48 (2001) 3-26) recites on page 18 that predicting the formation of solvates of a compound and the number of molecules of solvent or water incorporated into the crystal lattice of a compound is complex and difficult. Guillory (in Brittain et al., NY:Marcel Dekker, 1999, pages 183-226, teach that solvates are formed by recrystallization of drug substances. However, not all compounds will form solvates.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparing the instant compound and its salts, does not reasonably provide enablement for preparing any and all unknown solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification fails to prepare any solvates or identify the solvates and hydrates obtained.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of a compound, its salts, hydrates and solvates.

State of the Prior Art

Predicting the formation of solvates and hydrates of a compound and the number of molecules of solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of compounds. Note section 3.4 of Vippaguanta et al.

The amount of direction or guidance and the presence or absence of working examples

The working examples in the specification fail to show how any solvates and hydrates are produced. Further, Guillory on page 199 recites that compounds originally crystallized as solvates can lose the solvent induced by heat or vacuum vaporization.

The breadth of the claims

The breadth of the claims is drawn to the preparation of the compound, its salts, hydrates and all solvate forms.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the process of preparing all unknown solvates.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

Claims 1, 3, 5, 6, 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The expression "optional substituent", "optionally substituted" and "carboxylic ester" are employed in claims 1,3,5,6,9 and 10 with no indication given as to what groups really are.

One should be able, from a reading of the claims, determine what that claim does or does not encompass.

Why? Because that claim precludes others from making, using, or selling that compound for 20 years. Therefore, one must know what compound is being claimed.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention

The nature of the invention is the preparation of compounds useful for treatment of cancers.

State of the Prior Art

Substituents, hydrocarbon and acyl can have very different properties. The groups tend to convert from less stable to more stable forms. No method exists to predict what group will work with any significant certainty.

The amount of direction or guidance and the presence or absence of working examples

The specification fails to describe any substituents or carboxylic esters. Groups often change into other forms during drug manufacture. Based on the unpredictability in the art, applicants are not entitled to any and all unknown substituents or carboxylic esters groups.

The written description is considered inadequate here in the specification. Conception of the intended groups should not be the role of the reader. Applicants should, in return for a 20 year monopoly, be disclosing to the public that which they know as an actual demonstrated fact. The disclosure should not be merely an invitation to experiment. This is a 35 USC 112, first paragraph. If you (the public) find that it works, I claim it, is not a proper basis of patentability. In re Kirk, 153 USPQ 48, at page 53.

The breadth of the claims

The breadth of the claims are drawn to all substituted and unsubstituted compounds.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the compounds and their unknown other forms being claimed.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant other forms are enabled by the instant application.

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

No enablement can be found in the specification for the treatment of all cancers.

The nature of the invention

The nature of the invention is drawn to the method of using the instant compounds in the treatment of cancer in which inhibition of Hsp 90 is required.

State of the Prior Art and the level of skill in the art

It is well recognized in the art that there is only a limited understanding of the activities of Hsp 90 as it relates to its particular biological functions. Zhao et al. (Biochem. Cell Biol., 83, pp. 703-710 2005) on page 703 recite that the mechanism of Hsp 90 function remains poorly understood. The number of identified Hsp90 client proteins is over 100 and is still quickly increasing. See Xiao et al.(Mini-reviews in Medicinal Chemistry, 2006, 6, 1137-1143) on page 1137. The art recognizes that specific some drugs may block progression of tumors and others will promote tumor formation. See Xiao et al. (Current Medicinal Chemistry, 2007, 14, 223-232) in section 6 on page 230 therein. Further, Chiosis (Expert Opin. Ther. Targets 10(1) 2006 ,

37-50) teaches that the genetic plasticity of cancer cells often permits rapid development of resistance, even in patients who initially respond to targeted agents such as imatinib.

Predictability/unpredictability of the art.

The high degree of unpredictability is well recognized in Hsp 90 inhibition. The role of Hsp 90 inhibitors in pancreatic cancer has not been studied. Note the abstract of Song et al. (Mol. Cancer Ther. 2008, 7(10), 2008). Xiao et al. on page 1140, states that Hsp90 inhibitors might be effective in killing end-stage tumors, but they might promote progression of early state tumors.The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles established that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any treatment regimen on its face.

The amount of direction or guidance and the presence or absence of working examples

The specification is silent as to whether if any compound treats all cancers..

The breadth of the claims

The breadth of the claims are drawn to the of any and all cancers.

The quantity of experimentation needed

In view of high degree of unpredictability in the art, the limited working example with no results and the fact that the breadth of the claims is not commensurate with that of any objective enablement and that the nexus between Hsp90 inhibition and all cancers has not been established, the quantity of experimentation needed would be undue when faced with the lack of

direction and guidance present in the instant specification in regards to the compounds and pharmaceutical compositions.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b). Applicants are also referred to In re Wands, 858 f.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in Ex parte Foreman, 230 USPQ 546 (Bd. Of App. and Inter 1986).

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 6, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expressions having hydrate, solvate, optional subsituents, optionally substituted and carboxylic ester in claims 1, 3, 5, 6, 9 and 10 are indefinite.

No antecedent basis can be found for "R_4 represents $CONR^B(Alk)_nR^A$" in claim 9 because Claim 1 does not permit the carboxamide to be substituted. No antecedent basis can be found for the variable R^C in claims 10 and 11. Further, the variables R^B and R^C are not defined in claim 1.

The claims measure the invention. United Carbon Co. v, Binney & Smith., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, "Claims measure invention and resolution of invention must be based on what is claimed".

The C.C.P.A. in 1978 held "that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim": In re Priest, 199 USPQ 11, at 15.

Information Disclosure Statement

The information disclosure statement filed April 6, 2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Patricia L. Morris/
Primary Examiner, Art Unit 1625

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